REMARKS

In the Final Action dated September 20, 2007, Claims 1-23, 25, and 44-68 are pending. Claims 44-57, 60, 62-63 and 65 are rejected under 35 U.S.C. §102(e) as by Esenaliev (U.S. Patent No. 6,165,440). Claims 1-14, 17, 19-22 and 25 are rejected under 35 U.S.C. §103(a) as unpatentable over Esenaliev. Claims 15-16, 18, 23, 58-59, 61, 64, and 66-68 are objected to as dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

This Response addresses each of the Examiner's rejections and objections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

By way of the foregoing amendments, Applicants have amended independent claims 1 and 2 to incorporate the subject matter of allowable claim 23. Claim 23 therefore has been canceled. Claims 44-68 have also been canceled, and claims 69-89 are added based on what the Examiner has indicated as allowable subject matter. No new matter is added by the foregoing amendments.

Regarding the §102(e) rejection of claims 44-57, 60, 62-63 and 65 based on Esenaliev, the rejection is rendered moot in view of the cancellation of these claims. Withdrawal of the rejection is respectfully requested.

With respect to the §103 rejection of claims 1-14, 17, 19-22 and 25, the Examiner maintains that Esenaliev teaches the use of nanoparticles with various forms of radiation for enhancing drug delivery to tumors. The Examiner also contends that Esenaliev discloses nanoparticles of a metal core in the range of 0.1 nm to about 7000 nm. The Examiner admits that Esenaliev does not expressly disclose that the radiation is in a form selected from the group

consisting of x-rays, microbeam arrays of x-rays, radioisotopes, electrons, protons, ion beams and neutrons, as claimed. Instead, Esenaliev indicates that the form of radiation is microwave, optical or RF, for example. However, the Examiner states that Applicants have not disclosed that the specified forms of radiation provide any advantage, are used for a particular purpose, or solve a stated problem. The Examiner is of the opinion that one of ordinary skill in the art would have expected Esenaliev's radiation and Applicants' invention, to perform equally well, allegedly because the radiation of both inventions would perform the same function of enhancing the effects of radiation and ablating a tissue or population of cells. Accordingly, the Examiner concludes that it would have been *prima facie* obvious to modify Esenaliev to arrive at the claimed invention as specified in claims 1 and 25, because such a modification would have been considered a mere design consideration which fails to patentably distinguish over Esenaliev.

Applicants respectfully disagree with the Examiner's rejection. Contrary to the Examiner's allegation, the radiation forms disclosed by Esenaliev do not perform the same function as the radiation forms recited in present claims 1-2. Further, the radiation forms recited in present claims 1-2 provide significant advantages over those disclosed by Esenaliev, and are not simply alternative design options.

Specifically, as submitted in the previous response, Esenaliev teaches irradiating particles by pulsed laser light (in the range of 0.2 μm to 2 μm) or microwaves to heat up the particles, or by ultrasound to agitate the particles. According to Esenaliev, the interaction of the laser, microwave, or ultrasonic radiation with the particles is only to produce cavitation, transient local heating, or acoustic streaming. These physical forces then function to disrupt membranes and interstitium (e.g., rupture tumor blood vessel walls and cancer cell membranes) to enhance delivery of macromolecular drugs into cancer cells. See col. 2, lines 30-38, col. 4, lines 37-52,

Fig. 1b, and Figs. 2-9 of Esenaliev. In contrast, according to the present invention, the nanoparticles absorb the energy from one or more of the recited forms of radiation and locally emit secondary ionizing electrons (in addition to fluorescent photons), which result in damage to surrounding tissue. Distinct from the forms of radiation taught by Esenaliev, the forms of radiation recited in the present claims do not cause heating or agitation of nanoparticles. Therefore, the radiation forms disclosed by Esenaliev do not perform the same function as the radiation forms recited in present claims 1-2. Further, those skilled in the art would have had no reason to look to the forms of radiation recited in the present claims, as they would not cause heating or agitation of nanoparticles to effect the therapeutic results as taught by Esenaliev.

With respect to Esenaliev's disclosure relating to the size of the metal core of nanoparticles, particles having a metal core of 7000 nm, i.e., 7 μm, are not nanoparticles, and are not believed to effectively penetrate tumor tissue.

Moreover, Applicants respectfully submit that the advantages of the claimed invention are evident in the results described in the application. The present application has shown that metal nanoparticles were able to access the whole tumor uniformly (Example 4, pages 30-31), and significantly enhanced the anti-tumor effects of a radiation therapy (Example 5, pages 32-33), evidencing a 86% tumor cure with gold nanoparticles versus 20% tumor cure absent gold nanoparticles. Such results achieved by the present invention are surprising and unexpected.

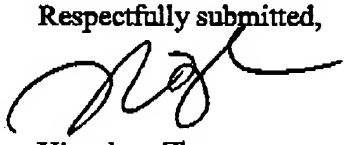
In view of the foregoing, Applicants respectfully submit that the claimed methods are not obvious over Esenaliev, and withdrawal of the §103 rejection is respectfully requested.

Applicants wish to direct the Examiner's attention to the amended claims presented above. Independent claims 1 and 2 have been amended to incorporate the subject matter of

allowable claim 23. New independent claim 69 is directed to a method of enhancing the effects of radiation by administering metal nanoparticles to an animal and subsequently irradiating the animal with radiation, wherein the nanoparticles are administered to the animal in an amount to achieve "a concentration in said tissue or said population of cells in the animal of at least about 0.1% metal by weight"; this concentration is delineate in previous claim 23. Independent claim 88 is directed to a method wherein the surface layer material comprises thioglucose. Independent claim 89 is directed to a method wherein the nanoparticles are polyanions of metals complexed with quaternary ammonium salts. Independent claims 69 and 88-89 are consistent with what the Examiner has indicated as allowable subject matter.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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